

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
1 July 2004 (01.07.2004)

PCT

(10) International Publication Number
WO 2004/055169 A3

- (51) International Patent Classification⁷: **G01N 33/53**, C12Q 1/34, 1/68, A61K 38/00
- (21) International Application Number: **PCT/US2003/039794**
- (22) International Filing Date: **15 December 2003 (15.12.2003)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:
60/433,096 13 December 2002 (13.12.2002) **US**
- (71) Applicant (for all designated States except US): **ELIXIR PHARMACEUTICALS, INC.** [US/US]; One Kendall Square, Building 1000-Fifth Floor, Cambridge, MA 02139 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **HUBER, Julie, L.** [US/US]; 39 Salisbury Road, Newton, MA 02458 (US). **SOLOMON, Jonathan, M.** [US/US]; 47 Winslow Avenue, Somerville, MA 02144 (US).
- (74) Agent: **MYERS, Louls**; Fish & Richardson P.C., 225 Franklin Street, Boston, MA 02110-2804 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report
- (88) Date of publication of the international search report:
23 December 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **CYTOCHROME C ACETYLATION**

(57) Abstract: Modulation of cytochrome c acetylation, e.g., with a SIR polypeptide, enables interventions that modulate lifespan regulation and cell proliferation, e.g., by modulating apoptosis and/or mitochondrial function such as respiration.

WO 2004/055169 A3

INTERNATIONAL SEARCH REPORT

International application No.:

PCT/US03/39794

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/53; C12Q 1/34, 1/68; A61K 38/00

US CL : 435/6, 7.7, 7.72, 18; 514/2

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/4, 6, 7.7, 7.71, 7.72, 7.91, 18; 514/2

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	YU et al. Induction of apoptosis in BCR/ABL+ cells by histone deacetylase inhibitors involves reciprocal effects on the RAF/MEK/ERK and JNK pathways. Cancer Biology & Therapy (United States). September-October 2003, Vol. 2, No. 5, pages 544-551, entire document.	1-21
A,P	CHEONG et al. Induction of apoptosis by apicidin, a histone deacetylase inhibitor, via the activation of mitochondria-dependent caspase cascades in human Bcr-Abl-positive leukemia cells. Clinical Cancer Research. 15 October 2003, Vol. 9, No. 13, pages 5018-5027, entire document.	1-21
A	RIEDER et al. The cytochrome c oxidase binding site on cytochrome c: Differential Chemical Modification of Lysine Residues in Free and Oxidase-Bound Cytochrome c. Journal Biological Chemistry. 10 September 1978, Vol. 253, No. 17, pages 6045-6053, entire document.	1-21
A	MARQUES et al. Hemeptide models for hemoproteins: the behavior of N-acetylmicroperoxidase-11 in aqueous solution. Journal Inorganic Biochemistry. 1999, Vol. 75, pages 281-291, entire document.	1-21

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

18 August 2004 (18.08.2004)

Date of mailing of the international search report

18 SEP 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Gabriele E. BUGAISKY

Telephone No. (571) 272-0700

INTERNATIONAL SEARCH REPORT

PCT/US03/39794

Continuation of B. FIELDS SEARCHED Item 3:

Dialog files 301, 305, 155, 5, 349 (Chemsearch, Merck Index, Medline, Biosis, PCT full text) WEST files USPT, PTPG, EPAB, DWPI, JPAB) search terms: cytochrome c, ferricytochrome c, ferrocytochrome c, microperoxidase, myohematin, hematin, acetyla?, deacetyla?, SIRT? silent information regulat?, apopto?